Serial Number: 09/504,389

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
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MARK W. PERLIN	)	
	)	
Serial No. 09/504,389	)	
	)	
Filed: February 15, 2000	)	A METHOD FOR DNA
	)	MIXTURE ANALYSIS
Art Unit: 1631	)	
	)	
Patent Examiner:	)	
	)	
John Brusca	)	

Pittsburgh, PA 15213

July 28, 2003

CERTIFICATE OF MAILING

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Ansel M. Schwartz
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7/30/03
Date

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

AMENDMENT

In response to the Office Action dated January 31, 2003, please enter the following amendments to the above-identified application as follows:

IN THE CLAIMS:

Please cancel Claim 21.

REMARKS

Claims 17-20 and 22-30 are currently active.

Claim Rejections - 35 U.S.C. 102

7. Claims 17-25, 29, and 30 were rejected under 35 U.S.C. 102(b) as being anticipated by Perlin et al.

Examiner suggests that the Perlin et al. paper describes the following items:

(i) shows on pages 1200-1204 a mathematical model of analysis of a mixture of pooled DNA molecules from a plurality of individuals by generation through a polymerase chain reaction of a short tandem repeat locus;

(ii) shows that it is possible to determine the genotype of a DNA molecule in the mixture by application of the method;

(iii) presents a mathematical method that comprises a matrix-vector analysis; and

(iv) shows methods of determining the optimum solution to obtain the correct genotype.

Examiner notes that with these described prior art items, claims 17-25, 29, and 30 could be viewed as having been anticipated by Perlin et al. However, if the Perlin et al. paper does not actually enable item (ii), then the ultimate step (d) of claim 17 -- "determining the genotype at a locus of an individual contained in the DNA mixture" -- would not be anticipated by the prior art described in Perlin et al.

Applicant demonstrates in the following that item (ii) is not enabled by the description on pages 1200-1204 of Perlin et al. This is accomplished by examining each of the four sections on pages 1200-1204 in the Perlin et al. paper, and looking for statements related to item (ii) -- the genotype at a locus of an individual contained in the DNA mixture can be determined by application of the method described in Perlin et al.

"Convolution Model" (p. 1200-1202). This section describes a general matrix-vector analysis method for "mathematically removing PCR stutter artifact from a genotyping experiment" by "deconvolving" (p. 1202, col. 1, para. 1). While this approach can determine the "genotype x of a diploid DNA sample" (p. 1201, col. 2, para. 1), it does not fully enable determining the genotype at a locus of an individual in a polyploid mixture (i.e., when there are two or more individuals present in the sample).

"The Single-Genotype Problem" (p. 1202-1203). This section specifically refers to "determination of a single genotype, i.e., the (up to) two alleles present in one individual's DNA at one marker" (p. 1202, col. 2, para. 1). Clearly this section on single-source, nonmixed DNA samples does not in itself enable determining the genotype of a DNA molecule in a mixture.

"Pooled DNAs for Population Studies" (p. 1203). The first paragraph of this section describes the utility of "pool[ing] together individual DNAs for PCR and/or gel readout" for applications that include determining "allele frequencies" or "linkage disequilibrium" (p. 1203, col. 1, para. 1). The second paragraph shows how to "recover the pooled allele frequency vector" (p. 1203, col. 1, para. 2) -- the paper makes no mention of determining the genotype at a locus of an individual in a mixture (the claimed invention), it only describes determining the allele frequency at a locus for a population in a mixture (the Perlin et al. prior art). The third paragraph describes six deconvolution algorithms (with optimal additional optimization) for solving this genotyping problem (p. 1203, col. 1, para. 3) -- the paper describes determining population allele frequencies, not determining the genotype of an individual. Nowhere in this section is enablement provided for the claimed invention "determining the genotype at a locus of an individual contained in the DNA mixture" (claim 17, step d).

"Pooled Markers Using Stutter-Based Encoding" (p. 1203-1204). This section describes a method that "enables the pooling of markers whose size ranges overlap" (p. 1203, col. 2, para. 6). However, the description and implementation refer to "the number of candidate diploid solutions" (p. 1204, col. 1, para. 3) -- that is, the (up to) two alleles present in one individual's DNA at one locus. Clearly this section on DNA samples for a one individual "diploid" situation does not enable determining the genotype for a mixture polyploid sample containing two or more individuals.

Applicant agrees with Examiner regarding the prior art items (i), (iii), and (iv) that are described by Perlin et al. However, Applicant can find no support for the candidate prior art item (ii). That is, Perlin et al. does not provide enablement for "determining the genotype at a locus of an individual in the DNA mixture" by application of the method. Therefore, Applicant respectfully submits that the ultimate step (d) of claim 17 -- "determining the genotype at a locus of an individual contained in the DNA mixture from the mathematical solution," where the DNA mixture contains two or more individuals -- is not anticipated by the prior art described in Perlin et al.

Applicant respectfully submits that these remarks fully address and adequately overcome examiner's objections, and requests that Claims 17-20, 22-25, 29, and 30 now be allowed.

8. Claims 17-25, 29, and 30 were rejected under 35 U.S.C. section 102 (b) as being anticipated by Perlin et al. Applicant arguments filed 26 November 2002 had stated that Perlin et al. does not show analysis of genotypes in a plurality of individuals. Examiner replied that Perlin et al. shows how such an analysis is facilitated by the disclosed method on page 1203.

Applicant examined the section specifically referred to by Examiner, "Pooled DNAs for Population Studies" (p. 1203). Applicant looked for support for the suggested "analysis of genotypes in a plurality of individuals" (Examiner remarks) as prior art that would in some way anticipate step (d) of claim 17 -- "determining the genotype at a locus of an individual contained in the DNA mixture from the mathematical solution."

(1) The first paragraph of this section on "Pooled DNAs for Population Studies" describes the utility of "pool[ing] together individual DNAs for PCR and/or gel readout." Applications include determining "allele frequencies" or "linkage disequilibrium" (p. 1203, col. 1, para. 1).

(2) The second paragraph shows how to "recover the pooled allele frequency vector" (p. 1203, col. 1, para. 2). No mention is made by Perlin et al. of determining the genotype at a locus of an individual in a mixture (the claimed invention), only how to determine the allele frequency at a locus for a population in a mixture (the candidate prior art).

(3) The third paragraph describes six deconvolution algorithms (with optimal additional optimization) for solving this genotyping problem (p. 1203, col. 1, para. 3). The enablement provided by Perlin et al. is determines population allele frequencies, not the genotype of an individual (the claimed invention).

Applicant agrees with Examiner that Perlin et al. "shows analysis of genotypes of a plurality of individuals" on page 1203. However, this analysis is strictly limited to determining population allele frequencies, and does not extend in any way to determining individual genotypes within that population. But the claimed invention refers to "determining the genotype at a locus of an individual contained in the DNA mixture from the mathematical solution" (claim 17, step d).

Applicant can find no support in Perlin et al. for any "analysis of genotypes in a plurality of individuals" (Examiner remarks) that enables "determining the genotype at a locus of an individual" (the claimed invention) in a mixed DNA sample. Therefore, Applicant respectfully submits that the ultimate step (d) of claim 17 -- "determining the genotype at a locus of an

individual contained in the DNA mixture from the mathematical solution" for a DNA mixture comprising two or more individuals -- is in no way anticipated by the prior art described in Perlin et al.

Applicant respectfully submits that these remarks fully address and adequately overcome examiner's objections, and requests that Claims 17-20, 22-25, 29, and 30 now be allowed.

Claim Rejections - 35 U.S.C. 103

10. Claims 17, 22, and 26-28 were rejected under 35 U.S.C. section 103(a) as being unpatentable over Perlin in view of Clayton et al.

Examiner notes that since (a) Perlin et al. could be viewed as enabling how "to determine the genotype of a DNA molecule" (Examiner remarks), i.e., the "genotype at a locus of an individual contained in the DNA mixture" (claim 17, step d), and (b) Clayton et al. show how mixture analysis can be used to "link suspected criminals to a crime scene" (Examiner remarks), it would have been obvious to one skilled in the art at the time the invention was made to use the method of Perlin et al. for analyzing the mixed forensic DNA samples described by Clayton et al.

Applicant agrees with Examiner that Perlin et al. "shows analysis of genotypes of a plurality of individuals." However, the Perlin et al. pooled DNA analysis is strictly limited to determining population allele frequencies, and does not extend in any way to determining individual genotypes within that population. But the claimed invention refers to "determining the genotype at a locus of an individual contained in the DNA mixture from the mathematical solution" (claim 17, step d).

Applicant has carefully reasoned in these Remarks (see above Section "Claim Rejections - 35 U.S.C. 103", specifically subsections 7 and 8) that there is no support in Perlin et al. that enables "determining the genotype at a locus of an individual contained in the DNA mixture" (claim 17, step d). Therefore, by direct application of this reasoning, Applicant respectfully maintains that the claimed invention in no way anticipates the prior art described in Perlin et al.

Since (a) Perlin et al. does not enable how to "determine the genotype at a locus of an individual contained in the DNA mixture" (claim 17, step d), there can be no feasible combination with (b) Clayton et al.'s using DNA mixtures to "link suspected criminals to a crime scene." Therefore, it would not have been at all obvious to one skilled in the art at the time the invention was made to use the method of Perlin et al. (which is inherently inoperable as a method in isolation for genotyping individuals in a DNA mixture) for analyzing the mixed forensic DNA samples described by Clayton et al. Since the combination could not work, there would have

been no obvious motivation (nor any feasible mechanism) to combine Perlin et al. and Clayton et al. in the way that Examiner suggests.

Applicant respectfully submits that these remarks fully address and adequately overcome examiner's objections, and requests that Claims 17, 22, and 26-28 now be allowed.

Double Patenting

11. Examiner notes that claim 21 is a substantial duplicate of claim 17. Claim 21 has been canceled.

14. Examiner provisionally rejected claims 17-30 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5-8, and 21 of copending Application No. 09/779096 in view of Perlin et al.

A terminal disclaimer has been filed in compliance with 37 CFR 1.321(c) to overcome the provisional rejection, since the conflicting application is commonly owned with this application.

In view of the foregoing amendments and remarks, it is respectfully requested that the outstanding rejections and objections to this application be reconsidered and withdrawn, and Claims 17-20, 22-30 now in this application be allowed.

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Respectfully submitted,

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